subjecting said yeast somatic components to nuclease digestion or alkali hydrolysis to decompose a high molecular-weight substance bound with polyamine wherein the amount of polyamine dissociated from said yeast somatic components is approximately double or more; and

recovering polyamine from said digested/hydrolyzed components.

REMARKS

Claim 1 has been canceled without prejudice. Claim 9 has been added. In Claim 9, support for the step of providing yeast somatic components can be found at line 22 of page 3 through line 4 of page 5, for example. Support for the decomposition step can be found at lines 5-23 of page 5, and lines 5-9 of page 3, for example. Support for the amount of dissociated polyamine can be found in the examples including line 5 of page 10, for example. Claims 2-8 have been amended solely to clarify the invention. Additionally, the specification has been amended to correct clerical errors. Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE." The amendments do not constitute the addition of any new matter to the specification. Applicant respectfully requests entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Specification

The specification has been amended to correct clerical errors in light of the Examiner's note.

Rejection Under 35 U.S.C. § 112

Claims 1-8 have been rejected under 35 U.S.C. § 112, second paragraph. Claim 1 has been canceled without prejudice. The remaining claims have been amended to clarify the phrases pointed out by the Examiner. Applicant respectfully requests withdrawal of this rejection.

Rejection Under 35 U.S.C. § 102

Claims 1, 3, and 5 have been rejected under 35 U.S.C. § 102 (b) as being anticipated by Nakabayashi. Claim 1 has been canceled without prejudice. Claims 3 and 5 have been amended to depend on new Claim 9. This rejection is moot.

Claim 1 and 3 have been rejected under 35 U.S.C. § 102 (b) as being anticipated by Sato. Claim 1 has been canceled without prejudice. Claim 3 has been amended to depend on new Claim 9. This rejection is moot.

Claims 1-5 and 8 have been rejected under 35 U.S.C. § 102 (b) as being anticipated by Tanekawa. Claim 1 has been canceled without prejudice. Claim 2-5 and 8 have been amended to depend on new Claim 9. This rejection is moot

Claims 1, 3, and 5 have been rejected under 35 U.S.C. § 102 (b) as being anticipated by Kanegae. Claim 1 ha2 been canceled without prejudice. Claims 3 and 5 have been amended to depend on new Claim 9. This rejection is moot.

Rejection Under 35 U.S.C. § 103

Claims 1-5 and 7-8 have been rejected under 35 U.S.C. § 103 as being unpatentable over Sato taken with Nakabayashi, Tanekawa, Ajinomoto, and Sugimoto. Claim 1 has been canceled without prejudice. Claims 2-5 and 7-8 have been amended to depend to new Claim 9. This rejection is moot.

Claim 6 has been rejected under 35 U.S.C. § 103 as being unpatentable over Sato taken with Nakabayashi, Tanekawa, Ajinomoto, Sugimoto, and further in view of Iijima and Stanzl. Claim 6 has been amended to depend to new Claim 9. This rejection is moot.

New Claim 9

Claim 9 has been added. Claim 9 could not be anticipated by or obvious over the above references as explained below.

In Claim 9, the first step is providing yeast somatic components. The references except for Sato ("secondary references") relate only to this step. That is, all of the processes described in the secondary references are for obtaining yeast RNA compositions such as yeast extracts used as flavoring agents or nutritious elements. No polyamine recovering step is disclosed.

In Claim 9, the above yeast somatic components are used as the starting material of the second step. In the second step, polyamine is dissociated from the yeast somatic components by decomposing a high molecular-weight substance bound with polyamine. This decomposition step is conducted by nuclease digestion or alkali hydrolysis. This specific step is in no way disclosed in the secondary references.

Thus, the secondary references give no suggestion of the recovering step in Claim 9, which is the third step.

Sato ("primary reference") discloses a polyamine recovering step. Sato is described in the present specification in the first paragraph of page 3. As described in the specification, under the acidic conditions of Sato, because a part of polyamine precipitates together with a high molecular-weight substance, all the polyamine contained in yeast could not be recovered. The acidic conditions are not sufficient to decompose a high molecular-weight substance bound with polyamine. This is clearly shown in Example 1 as compared with Comparative Example 1 (corresponding to Sato).

	Starting Material	Second Step	Yield per kg of yeast
Example 1	Yeast extract	Acid treatment + Nuclease digestion (25°C for 15 hours)	465 mg polyamine per 698 mg composition
Comparative Example 1 (Sato)	Yeast extract	Acid treatment	155 mg polyamine per 500 mg composition

In Example 1 as compared with Comparative Example 1, surprisingly, the amount of dissociated polyamine is more than double (300%).

Similarly, Examples 2 and 3 show significant effects as compared with Comparative Examples 2 and 3.

	Starting Material	Second Step	Yield per kg of yeast
Example 2	Physical crushed yeast somatic components	Nuclease digestion (37°C for 18 hours)	87 mg polyamine per 183 mg composition
Comparative Example 2	Physical crushed yeast somatic components	None	42 mg polyamine per 220 mg composition

	Starting Material	Second Step	Yield per kg of yeast
Example 3	Yeast RNA composition	Alkali hydrolysis (0.3N, 37°C for 18 hours)	1460 mg polyamine per 1750 mg composition
Comparative Example 3	Yeast RNA composition	None	460 mg polyamine per 550 mg composition

In Examples 2 and 3 as compared with Comparative Examples 2 and 3, respectively, surprisingly, the amounts of dissociated polyamine are more than double (210% and 320%, respectively).

The secondary references are directed to yeast somatic components themselves, and the primary reference is directed to polyamine obtained from yeast somatic components, such as those disclosed in the secondary references, used as the starting material. There is no motivation or suggestion to combine these references. Further, due to the second step of the present invention, a significantly high yield of polyamine can be achieved, which the primary reference or the secondary references never achieved.

"To establish a *prima facie* case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. If an independent claim is nonobvious under 35 U.S.C. § 103, then any claim depending therefrom is nonobvious." (M.P.E.P. § 2143.03). Thus, Claim 9 could not be obvious over the prior art, and at least for the reasons described above, the remaining claims also could not be obvious over the prior art. Applicant respectfully requests withdrawal of the rejections.

CONCLUSION

In light of the Applicant's amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

The paragraph beginning at line 15 of page 5 has been amended as follows:

The paragraph beginning at line 5 of page 2 has been amended as follows:

As examples of using polyamine for food, konnyaku (a jelly-like food made from the starch of devil's tongue) to which spermidine and spermine are added to reduce a smell peculiar to konnyaku and which does not have a bad effect if it is cooked with other foods (Japanese Patent Laid-open No.1994-38690) and a polyamine-mixed nutritional composition to which polyamine is mixed to accelerate protein absorption for the purpose of maintaining satisfactory growth and health conditions (Japanese Patent Laid-open No.1994-305956) and others have been proposed. In addition, as examples of using polyamine as medicines, a method of stopping gastric acid secretion and a composition for intake for the purpose of stopping gastric acid secretion (Japanese Patent Laid-open No.1983-131914) and immune activator (Japanese Patent Laid-open No.1984-98015 and Japanese Patent Laid-open No.1990-223514) and others have been proposed.

The paragraph beginning at line 17 of page 2 has been amended as follows:

Incidentally, it is known that meats and fermented foods such as cheese and miso (soybean paste) contain more polyamine than do milk and vegetables (Bardocz, S. et al., J. Nutr. Biochem., vol.4, p.66, 1993; Polyamine Society 12th Meeting for Reading Research Papers Lectures Outline, p.4, 1995). Consequently, the amount of polyamine contained in nutritional compositions of infant formula and others, of which milk is the main ingredient, is very small. Additionally, it was reported that human milk contained a relatively large amount of polyamine (Japanese Journal of Pediatric Gastroenterology and Nutrition, vol.1.9, no.2, pp.115-121, 1995) and it can be said that it is preferable from a physiological point of view to enrich polyamine in nutritional compositions with a low polyamine content.

The paragraph beginning at line 1 of page 3 has been amended as follows:

Moreover, a method of manufacturing polyamine from yeast and a nutritional composition to which polyamine manufactured by this method is mixed have been proposed

(Japanese Patent Laid-open No.1998-52291). In this method, polyamine without an offensive smell and taste can be manufactured by treating yeast under acidic conditions. However, under acidic conditions, because a part of polyamine precipitates together with a high molecular-weight substance, all the polyamine contained in ~~the~~ yeast could not be recovered. Additionally, a part of polyamine is bound in vivo with a high molecular-weight substance, not all polyamine could be recovered simply by performing fractionation.

The paragraph beginning at line 24 of page 7 has been amended as follows:

As a method for membrane fractionation, for example, using an ultrafilter membrane (UF) of cellulose, cellulose acetate, polysulfone, polyamide, polyacrylonitrile, poly (4-ethlene fluoride), polyester, polypropylene and others with the fractionation molecule weight within the range of 1,000~100,000, UF of a polyamine solution is conducted and transmitted liquid containing polyamine is recovered. Another method that can be used for desalting is to perform nanofiltration (NF) of the polyamine solution using an NF membrane with a salt blocking coefficient of 30~80%.

IN THE CLAIMS:

Claims 1 and 3 have been canceled.

Claims 2-5 and 7-8 has been amended as follows:

2 (Amended) The method according to Claim ~~1~~9, wherein said nuclease is a nuclease contained in the yeast somatic components.

3. (Amended) The method according to Claim 9~~1~~, wherein the yeast somatic components are ~~prepared~~obtained from ~~bread yeast, wine yeast, beer yeast, torula yeast and others~~yeast selected from the group consisting of *Saccharomyces cerevisiae* and *Candida utilis*~~, by physically crushing, by using hot water, or by autolization~~.

4 (Amended) The method according to Claim ~~1~~9, wherein the decomposition step is conducted by digesting the yeast somatic components ~~are digested~~ with nuclease added to a solution containing the yeast somatic components, ~~wherein the solution is treated~~ at a pH value of 3~10 and at a temperature of 10~~-~~70°C.

5. (Amended) The method according to Claim ~~1~~9, wherein the decomposition step is conducted by hydrolyzing at 20-100°C the yeast somatic components ~~are hydrolyzed~~ with alkali added to a solution containing the yeast somatic components ~~to make it~~at a normality of 0.1~~-~~5N~~,~~ ~~wherein the solution is treated at 20~100°C~~.

6. (Amended) The method according to Claim ~~3~~9, wherein the yeast somatic components are ~~extracted~~an extract obtained by physically crushing yeast using a high-pressure homogenizer and an ultrasonic disintegrator.

7. (Amended) The method according to Claim ~~3~~9, wherein the yeast somatic components are ~~extracted~~an extract obtained from yeast using hot water at a pH value of 4~8 and at a temperature of 90~100°C, wherein ~~a common salt~~sodium chloride is added to a yeast suspension with a yeast concentration of 5~25% to make a salt concentration of 1~10%.

8. (Amended) The method according to Claim ~~3~~9, wherein the yeast somatic components are ~~extracted~~an extract obtained by autolyzing yeast~~, while accelerating autolysis by adding an autolysis accelerator~~.

Claim 9 has been added.

9 (New) A method of manufacturing a polyamine composition, comprising the steps of:

providing yeast somatic components selected from the group consisting of extracts obtained from yeast by physical crushing or autolysis or with hot water, and yeast RNA compositions;

subjecting said yeast somatic components to nuclease digestion or alkali hydrolysis to decompose a high molecular-weight substance bound with polyamine wherein the amount of polyamine dissociated from said yeast somatic components is approximately double or more; and

recovering polyamine from said digested/hydrolyzed components.